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CONTINUOUS VERSUS PULSED DEXAMETHASONE PHONOPHORESIS IN MANAGEMENT OF TMD. A COMPARATIVE CLINICAL STUDY

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ABSTRACT

Aim: The aim was to Compare the clinical outcome (pain score and mouth opening) of dexamethasone phonophoresis in a (continuous versus pulsed maneuver) for management of TMD.

Materials and participants: Eighty patients were diagnosed with temporomandibular disorder(internal derangement) then were equally divided into either of the 4 groups according to the gel and type of phonophoresis to be applied each patient was treated with 10 sessions over a total of 30 days as following: Group DCP (n=20 patients), who received dexamethasone and continuous phonophoresis, Group DPP (n= 20 patients), who received dexamethasone and pulsed phonophoresis, Group ACP (n=20 patients) who received acoustic gel and continuous phonophoresis and Group APP (20 patients) who received acoustic gel and pulsed phonophoresis. Pain and interincisal distance both before and after treatment were recorded and statistically analyzed.

Results: intergroup and intragroup comparisons were performed; a significantly lower pain score for all four study groups following treatment was observed however; DCP group showed significantly lower pain score than ACP and APP. Mouth opening showed no statistical significance in between all four groups after treatment while a significant higher mouth opening was shown before and after treatment indicating that all interventions resulted in significant increases in mouth opening, but no method was statistically superior to the others.

Conclusion: Both treatment modalities (continuous or pulsed) ultrasound therapy with and without dexamethasone gel application were effective in pain alleviation and improving interincisal distance however; Continuous dexamethasone phonophoresis was superior in pain relief.

KEY WORDS: Temporomandibular disorders, dexamethasone, phonophoresis.

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INTRODUCTION

The temporomandibular joint (TMJ)is the site where the mandible articulates with the cranium, is one of the most complex joints in the body. Disorders of this important joint involves pathologies of the joint, their muscles, and related structures. ^(1,2)

It has twenty-five percent prevalence; of whom up to seven percent of this population suffer pain and limited mouth movement that leads patients to pursue treatment. Many factors can cause TMD as infection, traumatic injuries, inflammation, congenital and / or developmental disorder, and neoplastic diseases, para-functional habits as teeth clenching and bruxism, or abnormalities of the intra-articular disk. (3,4) TMD is characterized by signs and symptoms that include pain, muscle tenderness, joint noises, and a limited range of motion⁽⁵⁾. The normal distance of mouth opening (inter-incisal distance) ranges from 53 to 58mm. patients with limited aperture will be presented with a 40 mm mouth opening might, whereas 35 mm mouth opening is a sign of disc displacement without reduction (6,7,8).

About 90% of TMDs can be treated with noninvasive, nonsurgical interventions, including occlusal splint therapy, correcting malocclusion, physical therapy, and psychology. ⁽⁹⁾ most probably in such cases a multidisciplinary approach is will be required to reach optimum management ⁽¹⁰⁾. Conservative treatment modalities of TMD includes; oral medication, physical therapy, orthodontic treatment and occlusal splinting. Physical therapy is an underestimated but effective treatment that alleviate pain and inflammation and to improves joint function ⁽¹¹⁾

Currently many electro-physical therapeutic modalities are being used to relief pain symptoms associated with TMD which includes one of which is ultrasound (US) therapy; a well-established modality in general for management of musculoskeletal pain which possesses thermal and non-thermal effects ¹² Temporomandibular joint framework consists of capsule, fascia, muscles and ligaments that are tissues of high collagen content which exhibit maximum absorption character. ^(13, 14). thermal energy provided by ultrasound waves induces local vasodilation, increasing cellular metabolism. A 40°C temperature rise in tissues for at 5 minutes is capable of achieving significant thermal effect. This thermal property not only provides pain relief but also reduces joint stiffness ⁽¹⁵⁾

More over; on a cellular level ultrasound US therapy induces mast cell degranulation, boosts protein synthesis, fibro-blast mobility, growth factor formation; Leading to pain relief and tissue regeneration and repair ⁽¹⁶⁾.

Recently pulsed ultrasound (PUS) has been included for treatment of TMDs showing interesting results of tissue regeneration via the mechanical loading of the condylar cartilage which leads to IL-1b expression, an important inflammatory cytokine closely related to TMD ⁽¹⁷⁾. Moreover, Uddin et al ⁽¹⁸⁾ demonstrated in an in- vitro studies that pulsed US can inhibit catabolic action of IL-1b that are known to stimulating chondrocytes proliferation and differentiation which in turn prevent cartilage destruction

In an animal study by Liang et al ⁽¹⁹⁾ PUS was used in rats with injury to condylar cartilage and proved that it can effectively manage sleep deprivation caused by such a case. Thus, PUS is an effective noninvasive modality in the treatment of TMDs.

Combined use of topical agents and phonophoresis results in more drug delivery into underlying tissues by ultrasound waves^(20, 21). It has been used with topical application of anesthetic agents, salicylate, NSAID, methyl nicotinate and steroids ⁽²²⁾ and proved to be one of the many advantageous modalities for the treatment of musculoskeletal disorders ^(23, 24, 25) Corticosteroids have long been effective drug in reducing inflammation in systemic disease and local tendon and/ or muscular inflammations. While they are mostly administrated orally, they have also been used trans-cutaneous that has faster distribution rate into the system once it has diffused into the skin, quickly reaching the capillaries and is carried out systemically. While the blood is moving through the capillaries, part of the corticosteroid diffuses to the surrounding tissues. This justifies investigating different maneuvers to enhance transcutaneous delivery, avoiding unnecessary prolonged drug contact. ⁽²⁶⁾

The null hypothesis is that no difference is found between dexamethasone gel phonophoresis with continuous or pulsed application of ultrasound on pain relief and inter-incisal distance in patients suffering from TMD.

AIM OF THE STUDY

Compare pain relief and mouth opening improvement following the used of dexamethasone phonophoresis in a (continuous versus pulsed maneuver) for management of TMD.

PARTICIPANTS AND METHODS

Ethical regulations

Ethical review and clearance was granted via Faculty of Dentistry's Ethics Committee in Minia University for performing the study under number (Ref: 94/ 739) date; 28/ 3/ 2023 and The trial was also registered on (www. Clinicaltrial.gov) under registration number ID (NCT06759584). All patients were informed about the steps, benefits, risks and the possible adverse effects of the proposed intervention before signing a written consent form.

Sample size calculation

The sample size was based on a previous published study ⁽²⁷⁾, using G power 1.3 Software for the primary outcome, the least possible number was

calculated; A total of 80 patients (20 each group) was decided via an impartial statistician not involved in the current study.

Participants

Consecutive sampling was done in the outpatient clinic of the Oral and Maxillofacial Surgery Department till the target population was achieved. Eighty patients suffering from TMD (27 males and 53 females) were carefully chosen. Inclusion criteria: patients of age ranging 20- 50 years old with persistent, recurring TMJ pain (Patients who showed 3 of the following: articular sounds, deviation of the jaw during the opening, restricted mouth opening, articular pain, facial and / or cervical muscle pain, and tenderness on palpation of the masticator muscle) for at least 3 months. Exclusion criteria: Patients with history of dexamethasone allergy, prior TMJ surgery or trauma to jaw, patient were also excluded if they have pacemakers, intra articular injections within the last 12 months, radiation therapy to head and neck region, skin lesion or scarred skin at the site of the upcoming procedure.

Grouping and Intervention

The participants (n=80) were randomly divided into four equal groups according to the gel and type of phonophoresis to be applied. Each patient was treated for one treatment cycle; with 10 sessions (1 session every 3 days for a total of 30 days) using ultrasound (SONOPULS 490; Germany) as following: Group DCP (n=20 patients); who received (5ml) dexamethasone gel 0.5 mg/g (Dexamethasone gel was prepared by colloid mill. The prepared gel was confirmed for proper drug content and concentration in - Faculty of Pharmacy- Mina University) and continuous phonophoresis, Group DPP (n= 20 patients), who received dexamethasone gel 0.5 mg/g. and pulsed phonophoresis, Group ACP (n=20 patients) who received acoustic gel (AQUATIOS GEL Ultrasound Gel / Misr Pharmaceuticals; Egypt) and continuous phonophoresis and Group APP (20 patients) who received acoustic gel and pulsed phonophoresis.

Using A patch test prior to the treatment drug allergy to dexamethasone was rule out. Following carefully cleaning of the pre-auricular skin of the affected TMJ 5 mm of acoustic gel was applied over the ultrasound head, and then 4 mm of the dexamethasone gel was applied over the skin. The sound head was applied with a light continuous circular motion over the skin of the affected joint.⁽⁹⁾

For continuous mode the parameters were set at 1 MHZ frequency and 1.5 watt/ cm² intensity for 5 minutes over the affected TMJ area while for the pulsed mode the same parameters were set at duty cycles of 20%.

Outcome

- Pain assessment: Pain scores was recorded on visual analog scale (VAS) ranging from 0 to 10 pain score where zero indicates no pain and ten indicated the worst pain the patient had ever felt (pretreatment as a base line mark and 30 days from the start of the treatment as the post- treatment assessment).
- Mouth opening assessment: measure of interincisal distance in millimeters (mm), before and after the treatment was completed.
- Both patient and assessor were blinded to the assigned treatment.

Data collection and statistical analysis

All the obtained values were tabulated and statistically analyzed via SPSS 10.0 statistical program. Quantitative variables were presented as means and standard deviations, while qualitative variables were presented as median and IQR. Wilcoxon signed-rank test was used for intragroup comparison of VAS and Mann -Whitney test was used for comparisons of VAS between the groups. Meanwhile; One Way ANOVA test was used to compare inter-incisal distance between the groups and a paired sample T-test was used to compare inter-incisal distance (pre and post) treatment within each group. The probability value of less than 0.05 was considered statistically significant.

Declaration of interests:

The study is self-funded and there is no conflict of interest to declare.

RESULTS

Ninety-three patients were assessed initially. Thirteen patients were excluded nine pts did not meet the inclusion criteria and four patients declined to participate. No patients were lost during the study or the follow up period. Consort flow diagram of the participants during the present clinical trial is shown in Fig (1).

The current study consisted of 53 female and 27 male patients suffering from TMDs divided in to four equal groups (n=20). Comparison of demographic characteristics (age and sex) across four groups: DCP, DPP, ACP, and APP, each with 20 participants indicates no statistically significant difference in age and sex distribution among the groups. These results indicate that the groups were well-matched in terms of age and sex. Tab (1)

Regarding the pain scores across the test groups; recording pain preoperatively and postoperatively. Postoperatively, statistically significant difference between groups was found (p = 0.020). Mann-Whitney tests revealed that the DCP group (median = 3, IQR = 2-3) had significantly lower VAS scores compared to both ACP and APP groups (both with median = 3, IQR = 3-4). The DPP group's scores (median = 3, IQR = 2.3-3) were not significantly different from any other group. Wilcoxon Signed rank tests showed highly significant reductions in VAS scores from preoperative to postoperative time points within all groups (all p < 0.001). These results suggest that while all interventions significantly reduced pain, the DCP method may be more effective in pain reduction compared to ACP and APP methods. Tab (2), Fig (2)



Fig (1): Consort Flow diagram for the study

		DCP	DPP	ACP	APP	
		No=20	No=20	No =20	No =20	P value
Age	Range	(20-60) ^a	(20-55) ª	(20-55) ^a	(20-59) ^a	0.721
	$MEAN \pm SD$	37.2±12.3	34.6±10.8	34.4±10	37.5±11.4	
Sex	Male	7(35%) ª	6(30%) ^a	7(35%) ª	7(35%) ^a	0.983
	Female	13(65%)	14(70%)	13(65%)	13(65%)	

TABLE (1) Comparison of demographic data between different groups

One Way ANOVA test for normally distributed quantitative data between the groups then by Post Hoc LSD test between each two groups

Chi square test for qualitative data between groups

Superscripts with different small letters refer to significant differences between each two groups Significant level at P value < 0.05

TABLE (2) Comparison of VAS between test groups at preoperative and postoperative time

N/A C		DCP	DPP	ACP	APP	
VAS		No= 20	No =20	No =20	No =20 No =20	- P value
Preoperative	Median IQR	7 ª (7-8)	8 ª (7-8)	7 ª (7-8)	7 ª (7-8)	0.705
Postoperative	Median IQR	3 a (2-3)	3 (2.3-3)	3ь (3-4)	3.5 ^b (3-4)	0.020*
P value		<0.001*	<0.001*	<0.001*	<0.001*	

Kruskal Wallis test for not normally distributed quantitative data between the four groups followed by Mann Whitney test between each two groups

Wilcoxon Signed rank test between preoperative and postoperative times within each group

Small letters Superscripts refer to significant differences between each two groups

*: Significant level at P value < 0.05



Fig. (2) Box plot showing the median of preoperative and postoperative pain score values for the four study groups

Mouth opening measurements; in mm; for the four study groups is shown in Tab (3) Fig (3), comparing preoperative and postoperative values. Preoperatively, there was no statistical significance between groups where p value of (0.876). Postoperatively, again, no statistical significance between groups was found with p value of (0.411). Regarding, paired samples t-tests within each group showed highly significant improvements from preoperative to postoperative measurements (all p<0.001). This suggests that all interventions resulted in significant increases in mouth opening, but no method was statistically superior to the others.

Mouth opening (mm)		DCP No =20	DPP No =20	ACP No =20	APP No =20	- P value
	$Mean \pm SD$	36.7±3.9	37.2±3.6	36.8±3.8	36.2±4.1	
Postoperative	Range	(39-50) ^a	(39-50) ^a	(38-48) ^a	(36-50) ^a	0.411
	$Mean \pm SD$	44.2±3.8	44.3±3.7	42.6±3.5	43.1±3.9	
P value		< 0.001*	< 0.001*	< 0.001*	< 0.001*	

TABLE (3) Comparison of mouth opening between test groups at preoperative and postoperative time

- One Way ANOVA test for normally distributed quantitative data between the three groups followed by Post Hoc LSD test between each two groups

- Paired Samples T test for normally distributed quantitative data between preoperative and postoperative times within each group

- Superscripts with different small letters refer to significant differences between each two groups

*: Significant level at P value < 0.05



Fig. (3) Bar chart showing mean of mouth opening preoperative and postoperative for the study groups

DISCUSSION

Pain alleviation, restoration of normal jaw movement and function, and restoration of normal lifestyle are all goals of treating temporomandibular disorder. The aim of the current study was to compare four different treatment modalities for management of TMDs.

Therapeutic (continuous or pulsed) ultrasound is a well-recognized physical therapy in the management of TMD. Though it is accepted among the clinicians and patients, it lacks standardization of the appropriate dosimetry, and duration.⁽¹²⁾ Phonophoresis is a method that enable enhanced diffusion of a topical agent into deep tissues by using ultrasound waves ^(20, 21). It has been used with topical application of anesthetic agents, NSAID, salicylate and steroids ⁽²²⁾. It is one of a variety of modalities proven to be useful in treatment of musculoskeletal disorders ^(23, 24, 25)

In the present study the dexamethasone used was a gel formula, applied in groups (DCP) and (DPP), rather than a cream formulation. This was based on previous study **Coskun et al** ⁽²⁸⁾ whom stated that the gel form is of higher ability to transmit acoustic waves than does the cream preparation due to its similarity to the US gel.

In Regards of the present study TMD is more frequent on females as it was stated by **Knezevic etal**⁽¹⁰⁾, **Rai etal**⁽²⁹⁾, and **Poveda-Roda etal**⁽³⁰⁾. There is an agreement amongst researchers that there is no clear explanation for the higher prevalence of TMD in female rather than males. **Poveda-Roda etal**⁽³⁰⁾ has suggested that this may be related estrogen as it increases awareness to pain stimulus by a neural activity in the central nervous system ⁽³⁰⁾

In our study preoperatively, all study groups showed no significant variation between groups (p = 0.705). Postoperatively, however, there was a statistically significant lower pain scores between groups (p = 0.020) revealing that the DCP group had significantly lower VAS scores compared to both ACP and APP groups. The DPP group's scores were not significantly different from any other group. It was also shown that a significant difference appeared preoperative to postoperative time points within all groups (all p < 0.001). These results suggest that while all interventions significantly reduced pain, the DCP method may of higher efficacy in relieving pain compared to ACP and APP methods. The results come in accordance with Sequeira and Girishan ⁽³¹⁾ whom found that hat phonophoresis therapy is more effective in controlling pain and increasing inter-incisal distance associated with TMDs than plan US therapy

In an Other study; researchers have found no significant difference between both diclofenac phonophoresis and ultrasound therapy in the treatment of myofascial pain syndrome as they were both similarly effective ⁽³²⁾

Studies by **Vijayalakshmi et al.** ⁽³³⁾ and **Deniz et al.** ⁽³⁴⁾ came to similar conclusions that phonophoresis is safe, reliable and efficient alternative for the management of TMD; investigating several clinical parameters marked improvements was reported with phonophoresis or therapeutic ultrasound in patients with TMJ pain, though phonophoresis therapy was superior to the other treatments.

Pottenger et al ⁽³⁵⁾ studied corticosteroid phonophoresis in Physical Therapy Clinics within the United States Army for the treatment of various myofascial pain disorders that affect the institute personal. The results showed high pain relief than did other applied treatments.

The use of ultrasound boosted the diffusion of topically applied compounds. Providing better outcome in a noninvasive method with minimum risk of injury to the liver and / or kidney from drug detoxification, and is better accepted by the patients.⁽³⁶⁾

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alleviated pain this may be attributed to both the thermal and non-thermal effects: The ultra- sound waves diffuse into the tissues locally causing heat generation within the high collagen content tissues; joint capsule, fascia and ligaments of the TMJ which exhibit maximum absorption, enhancing local vasodilation and increasing cellular metabolism. ^(13, 14) On the other hand the non-thermal effects of ultrasound allow for cavitation and acoustic streaming phenomena on the micro-environmental gases present within the tissue fluids. physical forces displace ions and small molecules results in uni-directional flow of fluid around cell membranes altering cellular permeability which is related to tissue regeneration enhancement. ^(14, 15).

Both thermal and non-thermal effects; boost up protein synthesis, enhance fibro-blast mobility, increase growth factor production; effectively reduce pain more over promote the regeneration and repair of the damaged tissues ⁽¹⁶⁾.

On the other hand, DCP group had significantly lower VAS scores compared to both ACP and APP groups this may be attributed to the diffusion of the dexamethasone in to the deep tissues, which is a profound anti-inflammatory, once it diffuses through the skin, part of the drug leaks into the TMJ surrounding tissues. This advantages not only avoiding unnecessary prolonged drug contact but leads to more pain reduction. ⁽²⁶⁾

Regarding mean mouth opening measurements comparing postoperatively no significant difference was found between groups with a p value of (0.411). Regarding, paired samples t-tests within each group showed highly significant improvements from preoperative to postoperative measurements (all p < 0.001). These results suggest that all interventions resulted in significant increases in mouth opening, but no method was statistically superior to the others which come in correlation with our previous primary outcome pain scores where there was a significant improvement in pain alleviation indication the decrease in inflammation of the TMJ surrounding tissues.

This comes in accordance with many researches ^(4, 10, 11, 16) one of which by Ter Haar ⁽³⁷⁾, whom stated the acoustic vibrations that alter the Ca / K ions concentrations gradient, which stimulate several cellular activity as; enhance of protein synthesis, increase fibroblastic mobility, and boosts up growth factor production. These cellular changes effectively reduce inflammation more over promote the repair the under lying tissues. Some authors suggest that microvascular hemodynamic changes; enhance perfusion, fibroblastic proliferation and the growth of precursor cells; lead to better repair and regeneration.

Further this comes in agreement with **Matheus etal** ⁽³⁸⁾ whom found a significant improvement in muscles stiffness when patients were treated with the ultrasound. Another possible mechanism is due to its impact on the nervous system, by nociceptor suppression which alters the large afferent fibers input into spinal cord leading to inhibition of endogenous processes of pain pathway which improves mouth opening; by altering pain perception locally at the joint ⁽³⁹⁾

All through the study there were no results to support that pulsed ultrasound therapy was significantly superior to the continuous UT, which may be due to the included patients sample; whom were suffering of chronic condition; according to **llter etal**⁽⁴⁰⁾ continuous ultrasound therapy is more efficient in pain alleviation than pulsed maneuver, in patients suffering myofascial pain. While; **Watson** ⁽⁴¹⁾ recommended assigning pulsed ultrasound therapy to treat acute pain while continuous ultrasound maneuver is more efficient for chronic pain. Similarly, low intensities are more effective for acute pain and higher intensities are used for chronic pain.

However, in regards to the pulsed ultrasound therapy, the post-operative pain and the mouth

opening were significantly improved in comparison with the preoperative status; this is supported by the fact that though the type of mode of ultrasound waves is pulsed it still delivers enough waves to the deep tissues to give the required function. This comes in accordance with Bombardo et al (42), Liu et al (43) and Ju et al (44); whom have elucidated that pain relief when using pulsed ultrasound therapy, either plain or phonophoresis, may be related to a decrease in the number of macrophages. Which can down regulate chemokines associated with macrophage accumulation as well as tumor necrosis factor and lipopolysaccharide involved in macrophage differentiation relieving pain and consequently allowing increased mouth opening. Thus the null hypothesis was rejected for the primary outcome (pain assessment) and accepted for the secondary outcome (improving mouth opening)

CONCLUSION

Both treatment modalities (continuous or pulsed) ultrasound therapy with and without dexamethasone gel application were effective in pain alleviation and improving inter-incisal distance. However; Continuous dexamethasone phonophoresis was more effective in relieving pain.

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